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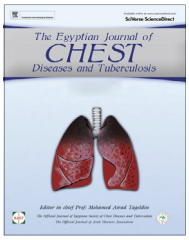

ORIGINAL ARTICLE

Developing prevention model of acute lung injury: Validity of lung injury prediction score and risk panel

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KEYWORDS

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Abstract *Background:* Acute lung injury (ALI) is an example of a critical care syndrome with few therapeutic modalities once the syndrome is fully established, and little has been done on the prevention of ALI.

Aim of the work: The aim of this work was to early identify the onset of acute lung injury (ALI) on admission and to prospectively evaluate the lung injury prediction score (LIPS).

Patients and methods: The study was carried out on 100 patients who aged >18 years, patients who had one or more of the acute lung injury (ALI) predisposing conditions on admission or within 6 h after were subjected to lung injury prediction score (LIPS).

Results: Acute lung injury developed in 15 patients, 11 patients (73.3%) had LIPS >3, while 4 patients (26.7%) had LIPS ⩽3 and only 4.70% of those who didn't develop ALI had LIPS >3, with a statistically significant relationship between patients above and below LIPS value of 3 ($P = 0.000$), LIPS cutoff value of ⩾3.5 on admission had a 73% sensitivity and 95% specificity with an area under the receiver operating curve of 0.883 (95% CI 0.782 to 0.984). Sepsis and pneumonia were the most frequent risk factors (60%).

Conclusions: Lung injury predictive score (LIPS) could early predict patients at risk to develop ALI on admission, Hyperbilirubinemia, high blood urea level and abnormal chest X-ray on admission were not included in the original LIPS but had significant association with development of ALI.

Introduction

Acute lung injury (ALI) and its more severe form acute respiratory distress syndrome (ARDS) are common and devastating complications after acute illness or injury with high morbidity and mortality, long term decrease in quality of life, and enormous cost related to intensive care and rehabilitation [1]. Acute lung injury is an example of critical care syndrome

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with limited treatment options once the condition is fully established. Despite improved understanding of the pathophysiology of ALI, the clinical impact has been limited to improvements in supportive treatment [2,3].

Surprisingly little research has been done on the prevention of ALI. Preliminary data suggest that ALI is rarely present at the time of hospital admission but develops over a period of hours to days in subsets of patients with predisposing conditions [4,5]. To this extent, ALI may be viewed as potentially preventable hospital complication similar to stress ulcer bleeding, venous thromboembolism or nosocomial infections [6].

It is likely that, inadequate and delayed recognition of patients at risk and the subsequent development of the full blown syndrome have obscured the therapeutic window [7]. ALI usually develops during the first hours of ICU admission, and often is the main reason for ICU admission [7]. On the other hand, the majority of patients with predisposing conditions never develop ALI and they may never been admitted to the ICU making the enrollment of unselected patients into ALI prevention studies neither feasible nor efficient [8]. A meaningful approach to ALI prevention therefore ought to be based on identifying patients at risk earlier than what is currently done (at the time of hospital admission, rather than ICU admission) [8].

Materials and methods

Study design

It was an observational cohort study, in which 100 patients admitted in Alexandria main University hospital with risk factors of ALI were enrolled in the study.

Inclusion criteria included

All patients who aged > 18 years who have one or more of the acute lung injury (ALI) predisposing conditions (Table 1) were included in the study, all patients who have been had any acute lung injury (ALI) risk factors before or 6 h after hospital admission were subjected to lung injury predictive score (LIPS) (Table 2) [9].

Acute lung injury will be defined based on the standard definition according to American-European consensus conference [11]:

(1) Acute onset of an insult known to cause ALI,
(2) Chest radiograph appearance,
(3) The ratio of partial pressure of oxygen in arterial blood to the fraction of inspired oxygen (PaO_2/FiO_2) (hypoxic index),
(4) Assessment of left atrial filling and pressure by means of a wedged pulmonary artery catheterization or clinical assessment.

Exclusion criteria included

(1) Acute lung injury or pulmonary edema already present at the time of hospital admission.
(2) Admitted for comfort or hospital care only.
(3) Patients admitted for cardiac telemetry, coronary care unit, and low risk elective surgery.
(4) Hospital readmission.
(5) Hospital transfer.
(6) Patients less than 18 years.

Table 1 Predisposing risk factors and risk modifiers: [9].

Risk factors	Measurement	Definition
Pneumonia	Yes/No	Consensus conference [25]
Sepsis	Yes/No	SCCM–ACCP definition [26]
Pancreatitis	Yes/No	Practice guidelines in acute pancreatitis [27]
Aspiration (pre-admission)	Yes/No	Inhalation of food or gastric contents [28]
High risk trauma	Lung contusion, smoke inhalation, near-drowning, multiple bone, brain injury	From Derdak [29]
High risk surgery	Aortic vascular, spine, thoracic, acute abdomen, Emergency	From Arozullah et al. [30,31]
Shock	Shock index; < 1, > 1 < 1.5, > 1.5	Heart rate (HR) divided by systolic blood pressure (SBP)
Risk modifiers		
Alcohol use	Yes/No, amount (number of drinks a week)	More than 2 drinks per day or a history of alcohol-related illness or admission [32,33]
Smoking	Never/former/current/number of pack-years	Substance abuse and mental health
Diabetes mellitus	Yes/No	Diabetes care 2009 [34]
Interstitial lung disease	Yes/No	ATS–ERS consensus classification of IIP [35]
Chemotherapy	Yes/No	Custom, cancer chemotherapeutic drugs during the 6 months prior to hospitalization
Tachypnea (respiratory rate > 30), Hypoalbuminemia		Based on the worst value during the first 6 h Serum albumin < 3.5 g/dL, the absence of measurement considered normal

Q7 **Table 2** Lung injury predictive score (LIPS) (Table 2) [10].

Variable	LIPS points		
Pneumonia	No = 0	Yes = 1	
Sepsis	No = 0	Yes = 1	
Aspiration	No = 0	Yes = 1	
Pancreatitis	No = 0	Yes = 1	
High risk trauma	No = 0	Yes = 1	
High risk surgery	No = 0	Elective = 1	Emergent = 3
Shock index	<1 = 0	>1<1.5 = 1	>1.5 = 2
Respiratory rate > 30	No = 0	Yes = 1	
Albumin < 3.5 g/dl	No = 0	Yes = 1	
Chemotherapy	No = 0	Yes = 3	
Alcohol > 2 drinks/day	No = 0	Yes = 1	
Smoking > 20 py	No = 0	Yes = 1	
ILD	No = 0	Yes = 1	
Diabetes	No = 0	Yes = −2	

LIPS >3 was considered high risk for developing ALI, and LIPS ⩽3 was considered low risk.

Data collection

All the patients included in the study were subjected to the following:

(1) Demographic data: age & sex.
(2) History taking: as regard the risk factors for acute lung injury.
(3) Complete clinical examination.
(4) Routine laboratory investigations including: complete blood count, serum sodium, serum potassium, serum creatinine, blood urea, random blood sugar, total protein, serum albumin, and serum bilirubin.
(5) Electrocardiogram (ECG) on admission and when needed.
(6) Chest X-ray on admission, every 24 h and when needed.
(7) Arterial blood gas analysis through direct arterial puncture or inserted arterial line for measurement of PaO_2 to calculate (PaO_2/FiO_2).
(8) Continuous arterial oxygen saturation (SpO_2) monitoring by pulse oxymetry. (Dash 4000 monitor, General Electric Medical System, Nell Cor) to detect any acute changes in oxygen saturation.
(9) Continous end tidal carbon dioxide (P_{ET} CO_2) monitoring using capnography. (Dash 4000 monitor, General Electric Medical System, Marquitte) to detect any acute changes in mechanical ventilation.
(10) Hemodynamic parameters:
    * Continuous monitoring of heart rate and mean systolic blood pressure using bedside monitor (Dash 4000 monitor, General Electric Medical System) and these were recorded every hour.
    * Central venous pressure monitoring (cm H_2O) every 6 h, was measured during connection to mechanical ventilator.
(11) Calculation of lung injury predictive score on admission.
(12) All patients fulfilling the criteria of acute lung injury (ALI) included in the study were mechanically ventilated according to same protocol recommended by ARDS network lung protective strategy [3]. All mechanically ventilated patients were will be managed with the same protocol for sedation and fluid management.

Outcome variables

(1) Development of acute lung injury (ALI).

Results

During the study period, 100 patients with eligible risk factors and no exclusion criteria were enrolled in the cohort and followed for development of ALI. A total of 15 patients (15%) developed ALI.

Gender

In our study most of the patients were males 64% while 36% were females with *male*: female ratio of 1.77:1.

Age

The age of the patients in the study ranged between 18 and 90 years with a mean of 48.38 ± 19.49.

Frequency of etiological factors of ALI

Pneumonia and sepsis were the most frequent predisposing factors for ALI in this study, amounting for 60% (9 patients) for each. This was followed by shock amounting for 53.4% (8 patients). Other etiological factors included aspiration (3 patients), high risk trauma (2 patients) and pancreatitis (1 patient) (Table 3).

Risk modifiers

Hypoalbuminemia in relation to ALI development
Hypoalbuminemia on admission was present in 13 (86.7%) from15 patients who had developed ALI, while it was present in only 29.4% of those who didn't develop ALI and there was a statistically significant relationship ($P = 0.000$) (Table 4).

RR > 30 in relation to ALI development
Among 15 patients who had developed ALI, 13 patients (86.7%) had RR >30 cycle/min on admission, while only 43.5% of those who didn't develop ALI had RR >30 cycle/

Table 3 Frequency of etiological factors of ALI.

	ALI group	
	No.	%
Pneumonia	9	60.0
Sepsis	9	60.0
Shock	8	53.4
Aspiration	3	20.0
High risk trauma	2	13.3
Pancreatitis	1	6.70

Table 4 Hypoalbuminemia in relation to ALI development.

		ALI development				Total	
		Yes		No			
		No.	%	No.	%	No.	%
Albumin	⩽3.5 g/dl	13	86.70	25	29.40	38	38.00
	>3.5 g/dl	2	13.30	60	70.60	62	62.00
Total		15	100.00	85	100.00	100	100.00
X^2		17.74					
P		0.000					

min on admission and There was a statistically significant relationship ($P = 0.002$).

Diabetes in relation to ALI development

From 15 patients who had developed ALI, 5 patients (33.3%) had diabetes on admission, while 31.8% of those who didn't develop ALI had diabetes on admission. There was no statistically significant relationship ($P = 0.561$) (Table 5).

Smoking in relation to ALI development

Among 15 patients who had developed ALI, 4 patients (26.7%) had history of smoking >20 packet per year (py) on admission compared to only 7.1% of those who didn't develop ALI and there was a statistically significant relationship ($P = 0.041$) (Table 6).

Certain risk modifiers like alcohol use, chemotherapy, and interstitial lung disease (ILD) were not assessed in our study because non of the included patients in the study have had any of these conditions.

Risk factors for developing ALI

Sepsis in relation to ALI development

Sepsis on admission was present in 9 patients (60%) Among 15 patients who had developed ALI, while only 30.6% of those who didn't develop ALI had sepsis on admission and there was a statistically significant relationship between sepsis and development of ALI, ($P = 0.03$) (Table 7).

Pneumonia in relation to ALI ALI development

From 15 patients who had developed ALI, 9 patients amounting for 60% had pneumonia on admission compared to only12 patients out of 85patients amounting for 14.1% of those who didn't develop ALI and there was a statistically significant relationship between pneumonia and development of ALI, ($P = 0.000$) (Table 8).

Shock index in relation to ALI development

Among 15 patients who had developed ALI, 4 patients (26.7%) of them had shock index > 1 < 1.5 on admission and the same number having shock index ⩾ 1.5, while only 28.3% of those who didn't develop ALI had shock index > 1 on admission. There was no statistically significant relationship between shock index and development of ALI, ($P = 0.139$) (Table 9).

Aspiration in relation to ALI development

From 15 patients who had developed ALI, 3 patients (20%) of them had aspiration on admission, compared to only 10.6% of those who didn't develop ALI and there was no statistically significant relationship ($P = 0.257$).

There were another important risk factors for developing ALI as trauma, major surgery, acute pancreatitis which were presented in our patients by small number of patients, Among 15 patients who had developed ALI, 2 patients (13.3%) had trauma on admission, and 1 patient (6.7%) had acute pancreatitis on admission but null of them had high risk surgery as risk factor for ALI on admission. There was no statistically significant relationship between these risk factors and development of ALI ($P = 0.389$) for acute pancreatitis and ($P = 0.143$) for trauma.

CXR on admission in relation to ALI development

8 out of 15 patients constituting 53.4% of those who developed ALI have had one or more lobe infiltrations in their CXR on admission compared to only 21 out of 85 patients constituting 24.7% of those who didn't develop ALI and there was a statistically significant relationship ($P = 0.009$) (Table 10).

Table 5 Diabetes in relation to ALI development.

		ALI development				Total	
		Yes		No			
		No.	%	No.	%	No.	%
Diabetes	Yes	5	33.3	27	31.8	32	32.00
	No	10	66.7	58	68.2	68	68.00
Total		15	100.00	85	100.00	100	100.00
X^2		0.014					
P		0.561					

Table 6 Smoking in relation to ALI development.

		ALI development				Total	
		Yes		No			
		No.	%	No.	%	No.	%
Smoking	> 20 py	4	26.70	6	7.10	10	10.00
	< 20 py	11	73.30	79	92.90	90	90.00
Total		15	100.00	85	100.00	100	100.00
X^2		5.447					
P		0.041					

Table 7 Sepsis in relation to ALI development.

		ALI development				Total	
		Yes		No			
		No.	%	No.	%	No.	%
Sepsis	Yes	9	60.0	26	30.60	35	35.00
	No	6	40.0	59	69.40	65	65.00
Total		15	100.00	85	100.00	100	100.00
X^2		4.848					
P		0.03					

Table 8 Pneumonia in relation to ALI development.

		ALI development				Total	
		Yes		No			
		No.	%	No.	%	No.	%
Pneumonia	Yes	9	60.0	12	14.1	21	21.00
	No	6	40.0	73	85.9	79	79.00
Total		15	100.00	85	100.00	100	100.00
X^2		16.179					
P		0.000					

Table 9 Shock index in relation to ALI development.

		ALI development				Total	
		Yes		No			
		No.	%	No.	%	No.	%
Shock index	> 1 < 1.5	4	26.7	14	16.5	18	18.00
	⩾1.5	4	26.7	10	11.8	14	14.00
	< 1	7	46.7	61	71.8	68	68.00
Total		15	100.00	85	100.00	100	100.00
X^2		3.94					
P		0.139					

Results showed that 28.6% of patients who developed ALI had significant ischemic changes in their ECGs in comparison to 16% of patients who didn't develop ALI but this didn't reach a statistically significant relationship between ischemic changes in the ECG and development of ALI, ($P = 0.219$).

There were many other parameters which were observed to have certain relationship with ALI, among all these parameters only heart rate ($P = 0.007$), total protein ($P = 0.002$), serum Albumin ($P = 0.000$), serum bilirubin ($P = 0.008$), blood urea ($P = 0.016$), follow up CXR ($P = 0.008$) and follow up hypoxic index ($P = 0.000$) which showed statistically significant relationship with development of ALI.

LIPS in relation to ALI development

The Results in this study showed that LIPS scores ranged from 0 to 7 (median 2.0), in the current study lung injury predictive score (LIPS) of ⩾3.5 was found to predict ALI development

Table 10 CXR on admission in relation to ALI development.

		ALI development				Total	
		Yes		No			
		No.	%	No.	%	No.	%
CXR on admission	1 lobe infiltration	4	26.70	17	20.00	21	21.00
	2 lobe	4	26.70	4	4.70	8	8.00
	Normal.	7	46.70	64	75.30	71	71.00
Total		15	100.00	85	100.00	100	100.00
X^2		9.428					
P		0.009					

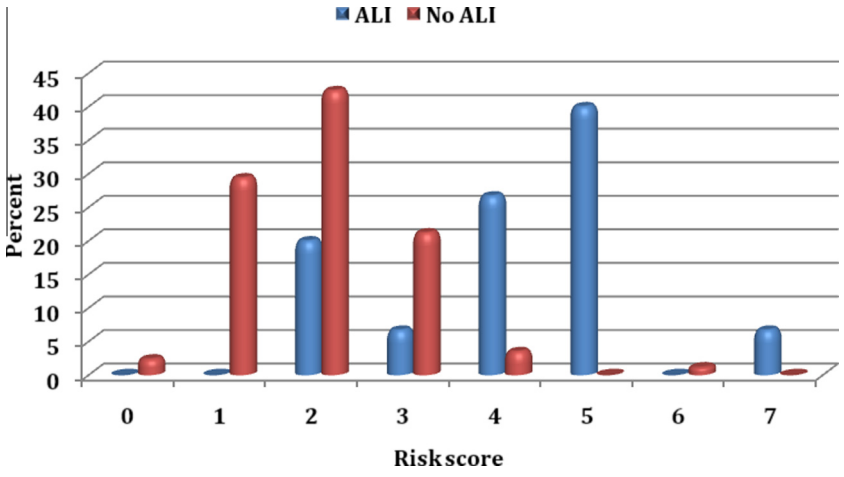

Figure 1 Frequency of ALI development across the range of the score.

with 73% sensitivity and 95% specificity (area under the curve 0.8).

The higher the risk score, the higher the incidence of ALI and there was a statistically significant relationship between the risk score and the development of ALI in the study population ($P = 0.000$) (Fig. 1) (Table 11).

Risk of ALI development in relation LIPS

It was found that 11 patients accounting for 73.3% of those patients who developed ALI had LIPS >3, while only 4 patients accounting for 26.7% had LIPS $\leqslant 3$ and only 4.70% of those who didn't develop ALI had LIPS >3, these findings resulted in a statistically significant relationship between patients above and below LIPS of 3 ($P = 0.000$) (Table 12).

2ry endpoint in relation to ALI development

Among 15 patients who had developed ALI, 2 patients had complete recovery, 3 recovered with residual complications and 10 had been died (Table 13).

ROC curve

Case processing summary

ROC curve: Shows an area under the receiver operating curve of 0.883 (95% CI 0.78 to 0.98), with a LIPS cutoff value of 3.5 predicting development of ALI, with 73% sensitivity and 95% specificity.

ALI developmet	Valid N (listwise)
Positive[a]	15
Negative	85
Missing	36

Larger values of the test result variable (s) indicate stronger evidence for a positive actual state.

[a] The positive actual state is 1.

Area under the curve

Test result variable(s): risk score

Area	Std. error[a]	Asymptotic sig.[b]	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
.883	.052	.000	.782	.984

The test result variable(s): risk score has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

[a] Under the nonparametric assumption.

[b] Null hypothesis: true area = 0.5.

Table 11 LIPS in relation to ALI development.

		ALI development				Total	
		Yes		No			
		No.	%	No.	%	No.	%
LIPS score	0	0	0.00	2	2.4	2	2.00
	1	0	0.00	25	29.40	25	25.00
	2	3	20.0	36	42.40	39	39.00
	3	1	6.70	18	21.20	19	19.00
	4	4	26.70	3	3.50	7	7.00
	5	6	40.0	0	0.00	6	6.00
	6	0	0.00	1	1.20	1	1.00
	7	1	6.70	0	0.00	1	1.00
Total		15	100.00	85	100.00	100	100.00
X^2		45.9					
P		0.000					

Coordinates of the curve

Test result variable(s): risk score

Positive if greater than or equal to[a]	Sensitivity	1 – Specificity
−1.00	1.000	1.000
.50	1.000	.976
1.50	1.000	.682
2.50	.800	.259
3.50	.733	.047
4.50	.467	.012
5.50	.067	.012
6.50	.067	.000
8.00	.000	.000

The test result variable(s): risk score has at least one tie between the positive actual state group and the negative actual state group.

[a] The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

Discussion

ALI can represent a devastating pulmonary process associated with increased length of stay, costs, and long-term poor outcomes [12,13]. Moreover, it represents a disease that has the potential to impart a burden across a younger and healthier population than previously recognized [14].

The incidence of ALI in this study was 15%, this finding was supported by Trillo-Alvarez et al. [15] in their study where of 409 patients out of 1707 patients who required ICU care during the study period, 68 (17%) developed ALI/ARDS. While the incidence was lower in other studies like Gajic et al. [16] where the incidence was 6.8% and Elie-Turenne et al. [17] where the overall incidence was 7%. This could be explained by the type of collected patients where in the current study and in the study of Trillo-Alvarez et al. the study was done in patients who required ICU admission while in the other two studies with the lower incidence rate the study was done in inward, ICU and ER patients.

The mean age in the current study was 48 years, in those who developed ALI it was 51.9 years and in those who didn't develop ALI it was 47.4 years with no significant statistical difference between the two groups (p value = 0.410). While some previous studies reported the increased risk of ALI in the elderly [18,19], other studies have not confirmed this association [20,21]. It could be argued that elderly patients seem to be more prone to sepsis, pneumonia and aspiration, and require more medical interventions. However, recent work implies that incidence of ALI/ARDS due to community-acquired pneumonia is lower in patients aged $\geqslant$85 yrs [20].

In the current study there was no significant difference regarding patient gender as a risk factor to develop ALI. This finding was supported by Ferguson et al. [22], Trillo-Alvarez et al. [15] and Elie-Turenne et al. [17] in their studies.

Regarding the risk factors for ALI development, in our study the incidence was higher in pneumonia (60% of the ALI group), sepsis (60% of the ALI group), shock (53% of

Table 12 Risk of ALI development in relation LIPS.

		ALI development				Total	
		Yes		No			
		No.	%	No.	%	No.	%
Risk of ALI	High (LIPS >3)	11	73.30	4	4.70	15	15.00
	Low (LIPS $\leqslant 3$)	4	26.70	81	95.30	85	85.00
Total		15	100.00	85	100.00	100	100.00
X^2		41.869					
P		0.000					

Table 13 2ry endpoint in relation to ALI development.

		ALI development		Total	
		Yes			
		No.	%	No.	%
2ry endpoint	Recovered	2	13.30	2	13.30
	Residual complication	3	20.00	3	20.00
	Died	10	66.70	10	66.70
Total		15	100.00	15	100.00

the ALI group) followed to a lesser degree by aspiration (20% of the ALI group) and trauma (13% of the ALI group), which was consistent with the results of the previous studies.

In most cohort studies and clinical trials, the majority of cases were caused by pneumonia followed by extrapulmonary sepsis, traumatic injuries, and shock [23,24].

The likelihood of ALI development depends not only on specific risk factors (from 5% with elective cardiopulmonary bypass [5] to 40% with septic shock [25]), but also on the presence of specific risk modifiers.

These risk modifiers included alcohol abuse [5], hypoalbuminemia [25,26], tachypnea [25,26], chemotherapy [27] and diabetes mellitus [25,28], although whether these factors were independent of one another wa unclear. This was consistent with the results of the present work except for Alcohol abuse and chemotherapy as there were no or too few people with these risk modifiers in the study population.

As regard to the risk modifiers in this work, hyperbilirubinemia was found as a determinate in progression to ALI, the mean serum bilirubin level in patients who developed ALI was 1.293 mg/dl compared to 0.498 mg/dl in those who didn't develop ALI with a statistically significant difference (p value = 0.008), this was similar to previously published work by Zhai R et al. [29]. This association could be explained by that high bilirubin level in the blood can induce cell lysis of erythrocytes, [30] and stimulate oxidative stress and decrease cell survival, [31] and promotes apoptosis in cultured cells [31,32].

The second risk modifier found to be of significant value in this study was hypoalbuminemia, mean serum albumin level in the patients who developed ALI was 2.44 g/dl, while it was 3.287 g/dl in those who didn't develop ALI (p value = 0.000), and there was a significant relationship between hypoalbuminemia and the development of ALI. This was consistent with the same findings in others studies [15–17].

This finding could be attributed to increased vascular permeability irrespective of underlying disease and fluid status by decreasing the oncotic pressure, so it can increase the risk to develop ALI [26,33].

Respiratory rate more than 30 cycle per minute was found to be a significant risk modifier associated with higher risk to develop ALI, (P value = 0.002) as 86.7% of those who developed ALI have RR > 30 cycle/min. This finding was supported by other studies having the same finding [15–17].This could be attributed to that most of ALI risk factors like pneumonia, sepsis, shock, aspiration were associated with tachypnea.

Diabetes mellitus (DM) was found to be one of the important risk modifiers, in the present study where there was no statistically significant relationship between diabetes and development of ALI (p value = 0.561), mean random blood glucose level was higher in patients who didn't develop ALI (204.35 mg/dl) compared to (166.8 mg/dl) in those who developed ALI (p value of 0.312). This finding was supported by many other studies [15–17]. It remains unclear, however, why the existence of diabetes mellitus confers protection to patients. Previous investigations have noted a lower incidence of ALI among diabetics compared to their non-diabetic cohorts. Honiden and Gong suggested that hyperglycemia as well as the therapeutic interaction of medications may alter the inflammatory response associated with ALI development [28,34].

An interesting finding in our study was that patients who developed ALI had higher heart rate (HR) on admission, the mean HR was 116.8 b/min compared to 100.3 b/min in those who didn't develop ALI (P value = 0.007). This was explained by the association of tachycardia with many risk factors of ALI, due to fever as in pneumonia and sepsis or a reflex to hypotension in shock and in trauma due to volume loss, pain, anxiety and infection.

As regard to the chest X-ray on admission, we found that patients with abnormal chest X-ray on admission were at higher risk to develop ALI than those with normal X-ray on admission (p value = 0.009), this might be explained by that X-ray abnormality was usually attributed to pneumonia which was a strong predictor of ALI development. Yoo et al. [35]in their study on patients with acute pancreatitis found that The risk of ARDS development was increased in patients with abnormal findings of chest X-ray on admission ($P < 0.05$). All these findings suggested that abnormal X-ray at admission was a strong independent predictor and risk factor for ALI development.

Cigarette smoking was found in our work to have a statistically significant relationship with development of ALI (P value = 0.041). In previous studies as in the work of Carolyn et al. [36] smoking was associated with high risk to develop ALI in patients with non- pulmonary sepsis, while in Calfee et al. [37] smoking was associated with high risk to develop ALI in patients with sever blunt trauma, in this study smoking was found to be an independent risk modifier for development of ALI.

High blood urea level was found to be associated with higher risk for development of ALI, mean blood urea level in the ALI group was 113 ± 90.954 mg/dl compared to 64.6 ± 66.4 mg/dl in those who didn't develop ALI (P = 0.016). Several studies had found a causal relationship between acute uremia and ALI and Several mechanisms have been suggested like; decreased alveolar fluid clearance, inflammatory cell infiltration and down regulation of pulmonary epithelial salt and water transporters including ENaC, Na, K-ATPase, and aquaporins [38–40].

Extra pulmonary sepsis was found in our study to be the most common risk factor that was associated with development of ALI. We found that there was a statistically

significant relationship between sepsis and ALI development (P value = 0.03) after comparing sepsis patients who developed ALI (60% of patients who developed ALI) with sepsis patients who didn't develop ALI (30.6% of those who didn't develop ALI), a finding consistent with many other studies [15,22]. Sepsis is considered one of the strongest predictors of ALI [23,24]. Rubenfeld et al. [41] in their study about incidence and epidemiology of ALI, a prospective population-based cohort study in 21 hospitals in and around King County, Washington, from April 1999 through July 2000, using a validated screening protocol to identify patients who met the consensus criteria for acute lung injury, found that the most common risk factor for ALI was severe sepsis with a suspected pulmonary source (46%), followed by severe sepsis with a suspected nonpulmonary source (33%). This finding was more or less compatible with findings in our study, where sepsis was the commonest risk factor for ALI.

Pneumonia, which is considered one of the sepsis syndromes, was found to be significantly associated with development of ALI in our study (P value = 0.000). This was supported by Rubenfeld et al. [41] and Sheu et al. [42] in their study to assess the influence of infection sites on development and mortality of ARDS, this finding was explained by the difference between the pathophysiology of direct and indirect lung injuries. The primary structure injured after a direct insult is the alveolar epithelium, while the first target of damage after an indirect insult is the pulmonary vascular endothelium [43]. When patients with pneumonia also develop sepsis, which was the case in 94% of our pneumonia patients, direct and indirect mechanisms may be triggered together, thus predisposing patients to a higher risk of developing ARDS.

We found that shock was the third most common risk factor in patients developing ALI (53%) but there was no statistically significant relationship neither with the development of ALI (p value = 0.139) nor with the primary end point (p value = 0.561). In Trillo-Alvarez et al. [15] Gajic et al. [16] and Elie Turenne et al. studies [17] shock was a common and statistically significant predictor of ALI. The difference between the results of our work and the others could be explained by our usage of Shock index (SI) or heart rate (HR) divided by systolic blood pressure (SBP) as a screening tool for shock in the study population, depending on heart rate as determinant to its value make it less specific marker of shock state and can be affected by other conditions like sepsis, pneumonia and other serious conditions.

It is interesting that conditions such as aspiration and pancreatitis were not stronger predictors in this cohort. The limited number of patients and presentation in most of them with less complicated disease may have dampened any resulting signal from severe cases of aspiration pneumonia or acute pancreatitis.

This preliminary study suggested that the risk of progression to ALI may be ascertained using the LIPS. The score and consequent degree of risk varies according to the type and number of predisposing conditions. Our aim was to validate the LIPS model in at-risk patients identified early in the course of the illness.

In the current study lung injury predictive score (LIPS) of $\geqslant 3.5$ was found to predict ALI development with 73% sensitivity and 95% specificity (area under the curve 0.8). This finding was different than that in Gajic et al. [44] where a score of $\geqslant 4$ predicted ALI development with 69% sensitivity and 78% specificity (area under the curve 0.8). This lower cutoff point is possibly due to the smaller sample size in our study and the narrow LIPS range in the current cohort (from 0–7) compared to (0–15) in the other study.

In our study the model accurately discriminated between the patients who did and did not develop ALI with an area under the receiver operating curve of 0.883 (95% CI 0.782 to 0.984). When compared to the previously published scoring methodology of LIPS, ability to discriminate patients who would go on to develop ALI was comparable in this study [9].

We believe that our results can facilitate the design and conduct of future ALI prevention strategies. Some of the results of these studies have been previously reported in the form of an abstract [10].

Assuming preventive strategies are identified, the LIPS had the potential to result in substantial morbidity and mortality reduction as well as cost savings. Specifically, LIPS of $\geqslant 3.5$ should prompt the clinician team to closely monitor the patient and communicate the potential need to address acute changes in respiratory status to the receiving service; this in turn would allow for the institution of preventive measures.

The transition of ALI studies from the ICU to the ED population may not only be prudent but obligatory as studies demonstrated the preponderance of ARDS cases were likely to stem from ED admissions secondary to insults exposed in the community. Hence, investigations evaluating the use of antiplatelet and statin therapies, a low tidal volume ventilation strategy, and restrictive transfusion in the ED may indeed be needed to mitigate ALI development [45,46]. Designed as a bundle, these interventions have the potential to curb the progression of illness in a patient identified at risk when instituted early.

The LIPS model utilized variables that were clearly defined and routinely available in the medical record. It didnot require testing beyond the standard of care and was not restricted to an ICU population. It identified patients early, at the time of hospital admission, and was validated for hospitalized patients irrespective of their required intensity of care at the time of admission.

Conclusion

The lung injury predictive score (LIPS) cutoff value of 3.5 on admission was associated with a 73% sensitivity and 95% specificity to predict development of ALI, LIPS had an excellent negative predictive value made it a useful screening tool to facilitate the identification of patients who can benefit from interventions to prevent disease progression. Pneumonia and sepsis were the most frequent risk factors that were significantly associated with ALI development. Hypoalbuminemia, tachypnea and cigarette smoking were risk modifiers that were significantly associated with high risk to develop ALI, and not included in the original LIPS cab be added to produce the modified lung injury prediction score.

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